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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/918,026	07/30/2001	Rosanne M. Crooke	ISPH-0588	1035

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EXAMINER

GIBBS, TERRA C

ART UNIT	PAPER NUMBER
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1635

DATE MAILED: 02/03/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

**Advisory Action  
Before the Filing of an Appeal Brief**

Application No.

09/918,026

Applicant(s)

CROOKE ET AL.

Examiner

Terra C. Gibbs

Art Unit

1635

**--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**

THE REPLY FILED 18 January 2006 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1. ☒ The reply was filed after a final rejection, but prior to or on the same day as filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:

- a) ☒ The period for reply expires 6 months from the mailing date of the final rejection.  
b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.

Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**NOTICE OF APPEAL**

2. ☒ The Notice of Appeal was filed on 18 January 2006. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

**AMENDMENTS**

3. ☒ The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because  
(a) ☒ They raise new issues that would require further consideration and/or search (see NOTE below);  
(b) ☒ They raise the issue of new matter (see NOTE below);  
(c) ☐ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or  
(d) ☐ They present additional claims without canceling a corresponding number of finally rejected claims.

NOTE: See Continuation Sheet. (See 37 CFR 1.116 and 41.33(a)).

4. ☐ The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).  
5. ☐ Applicant's reply has overcome the following rejection(s): \_\_\_\_\_.  
6. ☐ Newly proposed or amended claim(s) \_\_\_\_\_ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).  
7. ☒ For purposes of appeal, the proposed amendment(s): a) ☒ will not be entered, or b) ☐ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.  
The status of the claim(s) is (or will be) as follows:  
Claim(s) allowed: \_\_\_\_\_.  
Claim(s) objected to: \_\_\_\_\_.  
Claim(s) rejected: 1,4-10,12 and 13.  
Claim(s) withdrawn from consideration: \_\_\_\_\_.

**AFFIDAVIT OR OTHER EVIDENCE**

8. ☒ The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).  
9. ☐ The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing of good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).  
10. ☐ The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

**REQUEST FOR RECONSIDERATION/OTHER**

11. ☒ The request for reconsideration has been considered but does NOT place the application in condition for allowance because:  
See Continuation Sheet.  
12. ☐ Note the attached Information Disclosure Statement(s). (PTO/SB/08 or PTO-1449) Paper No(s). \_\_\_\_\_.  
13. ☐ Other: \_\_\_\_\_.

Continuation of 3. NOTE: The proposed amendment will not be entered because it raises new issues that would necessarily require further consideration and/or search. Applicant's proposed amendment recites an antisense oligonucleotide 12 to 30 nucleobases in length targeted to the coding region of a nucleic acid molecule encoding human acyl CoA cholesterol acyltransferase-2 (SEQ ID NO:3) in claim 1. This newly recited length, 12 to 30 nucleobases, has not been specifically recited before. Although the length of 8 to 50 has been searched, the newly recited shorter length has not been separately searched. Thus, Applicant's proposed amendment to the newly specified length would necessarily require a new sequence search to be performed for an antisense oligonucleotides 12 to 30 nucleobases in length. Further, the limitation "12 to 30 nucleobases" appears to be new matter since the instant specification at page 12, lines 34 and 35 recites, "from about 12 to about 30 nucleobases". In summary, since said length of 12 to 30 nucleobases has not been recited in any claims examined heretofore, the newly proposed claims specifying this length would require a new search and raise new prior art issues not previously considered. Further, no support for the specific limitation "12 to 30 nucleobases" could be found in the originally filed specification or claims as originally filed and therefore, this limitation appears to be new matter.

Additionally, the proposed amendment will not be entered because it recites an antisense oligonucleotide targeted to the coding region of a nucleic acid molecule encoding human acyl CoA cholesterol acyltransferase-2 (SEQ ID NO:3), wherein said antisense oligonucleotide inhibits the expression of a nucleic acid molecule encoding acyl CoA cholesterol acyltransferase-2 by at least 55% in claim 1. This newly recited percentage, but at least 55%, has not been specifically recited before. Although the percentage of by at least 60% has been searched, the newly recited percentage has not been separately searched. Thus, Applicant's proposed amendment to the newly specified percentage would necessarily require a new search to be performed for an antisense oligonucleotide targeted to the coding region of a nucleic acid molecule encoding human acyl CoA cholesterol acyltransferase-2 (SEQ ID NO:3), wherein said antisense oligonucleotide inhibits the expression of a nucleic acid molecule encoding acyl CoA cholesterol acyltransferase-2 by at least 55%. Further, the limitation "by at least 55%" appears to be a new matter issue because there is no support in the instant specification as filed for inhibiting the expression of acyl CoA cholesterol acyltransferase-2 "by at least 55%".

The proposed amendment filed January 18, 2006 indicates that support for the limitation, "inhibits the expression of a nucleic acid molecule encoding acyl CoA cholesterol acyltransferase-2 by at least 55%" is present throughout the specification, at Table 1, and at Table 2. First, it is noted that Table 2 discloses antisense molecules that inhibit mouse acyl CoA cholesterol acyltransferase expression and is thus irrelevant to the claims as filed, since the instant claims are drawn to antisense molecules that inhibit human acyl CoA cholesterol acyltransferase-2. Second, Table 1 shows approximately 23 specific antisense oligonucleotides which inhibit expression of human acyl CoA cholesterol acyltransferase-2 from 0% to 89%. Additionally, page 87, lines 29-32 recites, "As shown in Table 1, SEQ ID NOs: 21, 23, 24, 25, 28, 29, 30, 31, 33, 34, 35, 36, 37, and 38 demonstrated at least 40% inhibition of human acyl CoA cholesterol acyltransferase-2 expression". It appears that Applicants have support for the limitation, "inhibits the expression of a nucleic acid molecule encoding acyl CoA cholesterol acyltransferase-2 by at least 40%", as recited for Table 1. However, it does not appear that Table 1, nor any other part of the instant specification supports the limitation, "inhibits the expression of a nucleic acid molecule encoding acyl CoA cholesterol acyltransferase-2 by at least 55%". Therefore, this limitation appears to be new matter.

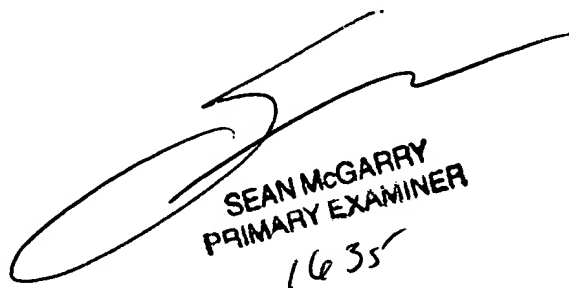
Continuation of 11. does NOT place the application in condition for allowance because: The request addresses the claims as amended, however the amended claims have not been entered on the record. However, if the proposed amendment was entered, claims 1, 4-10, 12, and 13 would remain rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement since the newly recited length, 12 to 30 nucleobases, appears to be new matter as discussed in the continuation to #3 above. Further, claims 1, 4-10, 12, and 13 would remain rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement since the newly recited percentage, by at least 55%, appears to be new matter as discussed in the continuation to #3 above.

Additionally, if the proposed amendment was entered, claims 1, 4-10, 12, and 13 would remain rejected under 35 U.S.C. 103(a) as being unpatentable over Oelkers et al., in view of Chong et al., and Bennett et al. [U.S. Patent No. 6,613,567]. In the proposed amendment filed January 18, 2006, Applicants traverse this rejection and argue that Bennett et al. is not a proper prior art reference since under 35 U.S.C. 103(c), the subject matter of the instant claims and the subject matter of Bennett et al. was owned by the same entity, and thus is not available for use as a 35 USC 102(e)-type reference. This argument is not found persuasive because contrary to Applicant's arguments, Bennett et al. would be available for use as a 35 USC 102(e)-type reference because Bennett et al. and the instant application have different inventors. For example, 35 USC 102(e) states, "A person shall be entitled to a patent unless —a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent". It is noted that Bennett et al. is a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent.

Applicants also argue that if Bennett et al. were a proper prior art reference, prior to the filing of the instant application, it was not clear to those of ordinary skill in the art whether specifically inhibiting only one of the two known acyl CoA cholesterol acyltransferase isoforms would be more advantageous than inhibition of the other isoform. For example, Applicants argue that Rudel et al. provide motivation to inhibit acyl CoA cholesterol acyltransferase-2 over acyl CoA cholesterol acyltransferase-1, since inhibition of the latter is shown to have toxic effects.

If entered, Applicant's arguments would not be found persuasive because the instant application has a filing date of July 30, 2001. It is noted that the Rudel et al. reference was published in June, 2005. It is the Examiner's position, that at the time of filing of the instant application, one of ordinary skill in the art would not have been motivated to target acyl CoA cholesterol acyltransferase-2 over acyl CoA cholesterol acyltransferase-1 since the toxic effects of the latter were only recently discovered. In summary, at the time of filing of the instant application, two isoforms of acyl CoA cholesterol acyltransferase were known, acyl CoA cholesterol acyltransferase-1 and acyl CoA cholesterol acyltransferase-2 (see Oelkers et al.). Also at the time of filing of the instant application, it was suggested to make acyl CoA cholesterol acyltransferase inhibitors (see Chong et al.). One of ordinary skill in the art would have envisioned and been motivated to make antisense inhibitors to either acyl CoA cholesterol acyltransferase isoforms, since Bennett et al. teach how to design

antisense compounds to different target regions of a known gene to inhibit gene expression at various capacities. Therefore, in combination, Oelkers et al., in view of Chong et al., and Bennett et al. render claims 1, 4-10, 12, and 13 obvious to one of ordinary skill in the art, as a whole, at the time the instant invention was made.



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